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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Assignee of Part interest: ChemGenes Corporation
Application Serial No.: 10/768,996
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Title: NOVEL OLIGONUCLEOTIDES AND RELATED COMPOUNDS
Art Unit: 1642
Examiner: Brandon J. Fetterolf, Ph.D.

CERTIFICATE OF EXPRESS MAILING UNDER 37 CFR 1.10

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3/3/07
Date

REPLY TO OFFICE ACTION

Commissioner for Patents
P.O.Box 1450
Alexendria, VA 22313-1450

Sir:

This reply is being filed in response to the Office action mailed on July 29, 2005, in conjunction with a petition to revive the above-referenced Nonprovisional Patent Application under 37 CFR 137(b) for unintentional delay. The Office action had communicated a restriction/election requirement between claims groups and species; a copy of the communication is enclosed.

The applicant hereby makes the following elections:

- Election between claim groups under 35 U.S.C. 121:
 - ☐ Applicant elects claims: Group I, claims 1-37.

- Species Election:
 - ❑ Applicant elects, with traverse, the antimetabolite agent Gemcitabine, 2'-deoxy, 2',2'-difluorocytidine, and submits below the reasons for disagreement on the restriction requirement between species.
 - ❑ Claims 1, 3-24, 26-37 are readable on the elected species.
 - ❑ Applicant submits that Claims 2 and 25 list other species of antimetabolite agents which, though not obvious variants of the species elected above or of each other, are related as disclosed in the context of the present invention and not distinct "species" within the meaning of 35 U.S.C. 121.

The Reasons for Disagreement on Restriction Requirement between Species

1. Unity of invention.

Unity of invention exists where compounds included within a Markush group share a common utility and share a substantial feature disclosed as being essential to that utility. MPEP Chapter 8, Section 803.02.

The present invention shows how to envelope nucleoside- and modified nucleoside- based anticancer agents and HIV related drugs as part of CpG oligonucleotides. While cancer and HIV related infections are distinct and different from each other, at the cellular level they share the pathology of genetic mutation and uncontrolled DNA synthesis: Uncontrolled growth of cells within the body due to known or unknown factors in the case of Cancer, and uncontrolled DNA synthesis and continued virus replication in the case of HIV due to the integration of viral genetic elements into human genetic elements. In both cases, damage to human DNA underlies the common pathology.

In either case, the key teaching of the invention applies, that is: How to control these uncontrolled processes by incorporating into the damaged DNA an antimetabolite prodrug, such as, an anticancer agent (in the case of cancer treatment) or an HIV inhibiting drug (in the case of HIV).

Extensive studies conducted as part of the search, research and development related to the invention and cited in the detailed specification on the anticancer drug Gemcitabine, show that the drug is phosphorylated within cellular environment before integration to damaged DNA. This process of phosphorylation within intracellular environment is enabled by the targeting of differentiated cells by the prodrug and the delivery of the drug to specific sites of damaged DNA. These same processes are envisaged for the other drug agents identified in claim 2 of the application.

It is expected, furthermore, that the CpG oligonucleotides of the invention will be effective in the treatment of different types of cancers (or HIV) by suitably selecting the anticancer agent (or HIV inhibitor). Examples of suitable drugs include: Floxuridine (CAS # 50-91-9) 5-Fluoro-2'-deoxyuridine for the treatment of colon cancer and Fludarabine (CAS # 21679-14-11) 2-Fluoro-9-b-D-arabinofuranosyladenine for the treatment of lymphocytic leukemia and lymphoma; and, HIV inhibitors Lamivudin (CAS# 134678-17-4) (2'-Deoxy-3'-thiacytidine) or Zidovudin (AZT) (CAS# 30516-87-1)(3'-Azido-3'-deoxythymidine) for HIV.

The results presented in the specification for Gemcitabine together with the structural similarity of the formulas S - [Gemcitabine]-[Link]- CpGn*CpG-Oligo-nucleotide and S - [Drug]-[Link]- CpGn*CpG Oligo-nucleotide lead to the expectation that drugs amenable to attachment to a CpGn*CpG-oligonucleotides will lead to valuable new drug intervention strategies for Cancer and HIV in the various embodiments of the invention.

For the prevalent cancer chemotherapeutic agents the promise of selective toxicity remains unfulfilled, since a target unique to cancer cells but absent in normal cells has eluded recognition. The requirement of the present invention that the oligonucleotides include at least two CpG moieties and a prodrug for an antimetabolite covalently linked to the oligonucleotide provides an approach for preferentially killing cancerous cells over non-cancerous cells. The rationale for CpG moieties carrying anticancer drug or HIV inhibiting drug is described in detail in the specification, along with the general structures of the formulas.

2. A reasonable number of species may be claimed in a single application.

Per 37 CFR 1.141, under appropriate circumstances, "more than one species of an invention, not to exceed a reasonable number, may be specifically claimed" in one national application.

Applicant suggests that the total number, 13, of compounds claimed in the categories of anticancer and HIV inhibitor agents is not unreasonably large, and furthermore, stands ready to amend the claims into appropriate format.

3. Special consideration given to Biotechnology applications

Per MPEP Chapter 8, Section 803.04, in order to "aid the biotechnology industry in protecting its intellectual property" the Director has waived the requirements of 37 CFR 1.141, *et seq.*, to permit a reasonable number (*normally* around ten) of nucleotide sequences to be claimed in a single application.

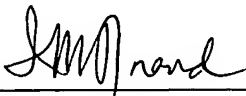
Given the fundamental unity of invention shown and the above stated policy consideration, the applicant believes that the number, 13, of claimed antimetabolite agents is reasonable.

For the reasons stated above, applicant respectfully requests reconsideration, and either withdrawal or modification of the restriction requirement between species.

In the case of any questions or deficiency in the compliance or fees, you are requested to kindly contact the undersigned representative.

Dated: March 3, 2007

Respectfully submitted,

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